Claims

1. A method of killing cancer cells, comprising administration to said cells of an effective amount of a c-FLIP inhibitor, wherein the c-FLIP inhibitor is administered as the sole cytotoxic agent in the substantial absence of other cytotoxic agents.

2. A method of treating cancer comprising administration to a subject in need thereof a therapeutically effective amount of a c-FLIP inhibitor, wherein the c-FLIP inhibitor is administered as the sole cytotoxic agent in the substantial absence of other cytotoxic agents.

3. A method of killing cancer cells having a p53 mutation, comprising administration to said cells of:
(a) a c-FLIP inhibitor and
(b) a chemotherapeutic agent, wherein the chemotherapeutic agent is a thymidylate synthase inhibitor, a platinum cytotoxic agent or a topoisomerase inhibitor.

4. A method of treating cancer associated with a p53 mutation comprising administration to a subject in need thereof
(a) a c-FLIP inhibitor and
(b) a chemotherapeutic agent, wherein the

chemotherapeutic agent is a thymidylate synthase inhibitor, a platinum cytotoxic agent or a topoisomerase inhibitor.

5. The method according to claim 3 or claim 4, further comprising administration of:
(c) a death receptor binding member.

6. The method according to claim 5, wherein the death receptor is FAS.

7. The method according to claim 6, wherein the binding member is the FAS antibody CH11.

8. The method according to any one of claims 3 to 7, wherein the chemotherapeutic agent is 5-FU, oxaliplatin or CPT-11.

9. The method according to claim 8, wherein the chemotherapeutic agent is 5-FU or oxaliplatin.

10. The method according to any one of claims 3 to 9, wherein the c-FLIP inhibitor and the chemotherapeutic agent are administered in a potentiating ratio.

11. The method according to claim 10, wherein the c-FLIP inhibitor and the chemotherapeutic agent are administered in concentrations sufficient to produce a CI of less than 0.85.

12. The method according to any one of claims 3 to 11, wherein the p53 mutation is such that p53 is completely inactivated in the cancer cells.

13. The method according to any one of claims 3 to 11, wherein the p53 mutation is a missense mutation resulting in the substitution of histidine (R175H mutation) or a missense mutation resulting in the substitution of tryptophan (R248W mutation) for arginine.

14. The method according to any one of claims 1 to 13, wherein said c-FLIP inhibitor is an RNAi agent, which modulates expression of a c-FLIP gene.

15. The method according to claim 14 wherein the c-FLIP inhibitor is an RNAi agent having nucleotide sequence
AAG CAG TCT GTT CAA GGA GCA (SEQ ID NO: 1) or
AAG GAA CAG CTT GGC GCT CAA (SEQ ID NO: 2)

16. The use of a c-FLIP inhibitor as the sole cytotoxic agent in the preparation of a medicament for treating cancer, wherein the medicament is for treatment in the substantial absence of other cytotoxic agents.

17. The use of
(a) a c-FLIP inhibitor and
(b) a chemotherapeutic agent, wherein the chemotherapeutic agent is a thymidylate

synthase inhibitor, a platinum cytotoxic agent or a topoisomerase I inhibitor in the preparation of a medicament for treating cancer associated with a p53 mutation.

18. The use according to claim 17, wherein the medicament further comprises:
(c) a death receptor binding member.

19. The use according to claim 18, wherein the death receptor is FAS.

20. The use according to claim 19, wherein the binding member is the FAS antibody CH11.

21. The use according to any one of claims 17 to 20, wherein the chemotherapeutic agent is 5-FU, oxaliplatin or CPT-11.

22. The use according to claim 21, wherein the chemotherapeutic agent is 5-FU or oxaliplatin.

23. The use according to any one of claims 17 to 21, wherein the c-FLIP inhibitor and the chemotherapeutic agent are present in a potentiating ratio.

24. The use according to claim 23, wherein the c-FLIP inhibitor and the chemotherapeutic agent are present in concentrations sufficient to

produce a CI of less than 0.85.

25. The use according to any one of claims 17 to 24, wherein the p53 mutation is such that p53 is completely inactivated in the cancer cells.

26. The use according to any one of claims 17 to 24, wherein the p53 mutation is a missense mutation resulting in the substitution of histidine (R175H mutation) or a missense mutation resulting in the substitution of tryptophan (R248W mutation) for arginine.

27. The use according to any one of claims 16 to 26, wherein said c-FLIP inhibitor is an RNAi agent, which modulates expression of a c-FLIP gene.

28. The use according to claim 27 wherein the c-FLIP inhibitor is an RNAi agent having nucleotide sequence
AAG CAG TCT GTT CAA GGA GCA (SEQ ID NO: 1) or
AAG GAA CAG CTT GGC GCT CAA (SEQ ID NO: 2).

29. A pharmaceutical composition for the treatment of cancer, wherein the composition comprises a c-FLIP inhibitor as the sole cytotoxic agent and a pharmaceutically acceptable excipient, diluent or carrier, wherein the composition is for treatment in the absence of other cytotoxic agents.

30. A pharmaceutical composition for the treatment of a cancer associated with a p53 mutation, wherein the composition comprises (a) a c-FLIP inhibitor
(b) a chemotherapeutic agent, wherein the chemotherapeutic agent is a thymidylate synthase inhibitor, a platinum cytotoxic agent or a topoisomerase I inhibitor
and
(c) a pharmaceutically acceptable excipient, diluent or carrier.

31. The composition according to claim 30, further comprising (c) a death receptor binding member.

32. The composition according to claim 31, wherein the death receptor is FAS.

33. The composition according to claim 32, wherein the binding member is the FAS antibody CH11.

34. The composition according to any one of claims 30 to 33, wherein the chemotherapeutic agent is 5-FU, oxaliplatin or CPT-11.

35. The composition according to claim 34, wherein the chemotherapeutic agent is 5-FU or oxaliplatin.

36. The composition according to any one of claims 30 to 36, wherein the c-FLIP inhibitor and the chemotherapeutic agent are present in a potentiating ratio.

37. The composition according to claim 36, wherein the c-FLIP inhibitor and the chemotherapeutic agent are present in concentrations sufficient to produce a CI of less than 0.85.

38. The composition according to any one of claims 30 to 37, wherein the p53 mutation is such that p53 is completely inactivated in the cancer cells.

39. The composition according to any one of claims 30 to 37, wherein the p53 mutation is a missense mutation resulting in the substitution of histidine (R175H mutation) or a missense mutation resulting in the substitution of tryptophan (R248W mutation) for arginine.

40. The composition according to any one of claims 29 to 39, wherein said c-FLIP inhibitor is an RNAi agent, which modulates expression of a c-FLIP gene.

41. The composition according to claim 40 wherein the c-FLIP inhibitor is an RNAi agent having nucleotide sequence

AAG CAG TCT GTT CAA GGA GCA (SEQ ID NO: 1) or AAG GAA CAG CTT GGC GCT CAA (SEQ ID NO: 2).

42. A kit for the treatment of cancer associated with a p53 mutation, said kit comprising (a) a c-FLIP inhibitor and (b) a chemotherapeutic agent, wherein the chemotherapeutic agent is a thymidylate synthase inhibitor, a platinum cytotoxic agent or a topoisomerase I inhibitor and (c) instructions for the administration of (a) and (b) separately, sequentially or simultaneously.

43. An RNAi agent having nucleotide sequence AAG CAG TCT GTT CAA GGA GCA (SEQ ID NO: 1) or AAG GAA CAG CTT GGC GCT CAA (SEQ ID NO: 2).

44. An RNAi agent consisting of nucleotide sequence AAG CAG TCT GTT CAA GGA GCA (SEQ ID NO: 1) or AAG GAA CAG CTT GGC GCT CAA (SEQ ID NO: 2).